

10/11/03

Access DB# 107816

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Paul Roberts Examiner #: \_\_\_\_\_ Date: 11/5/03  
Art Unit: 3731 Phone Number 30 5-7558 Serial Number: 091973335  
Mail Box and Bldg/Room Location: 2108 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*  
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Composite tissue adhesive

Inventors (please provide full names): soltz et al

Earliest Priority Filing Date: 10/14/01

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Claim 1. Need collagen concentration 300mg/ml - 800mg/ml  
as an adhesive

## STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher: <u>John Sim</u>	NA Sequence (#) _____	STN <u>✓</u>
Searcher Phone #: <u>308-4836</u>	AA Sequence (#) _____	Dialog <u>✓</u>
Searcher Location: <u>ELC 3700</u>	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: <u>11/10/03</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: <u>60</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: <u>50</u>	Other _____	Other (specify) _____



# **STIC Search Report**

**EIC 3700**

**STIC Database Tracking Number: 107816**

**TO: Paul Roberts**  
**Location: cp2 2a08**  
**Art Unit: 3731**  
**Monday, November 10, 2003**

**Case Serial Number: 09/973335**

**From: John Sims**  
**Location: EIC 3700**  
**CP2, 2C08**  
**Phone: 308-4836**

**john.sims@uspto.gov**

## **Search Notes**

Paul: I find some references to collagen at lower concentrations. Also a reference to "500-1500 ABC units" of collagenase; apparently ABC is a proprietary measurement of Advanced Biofactures Curacao, since I can't find any independent definition of an ABC unit.



# STIC Search Results Feedback Form

**EIC 3700**

Questions about the scope or the results of the search? Contact *the EIC searcher or contact:*

**John Sims, EIC 3700 Team Leader**  
**308-4836, CP2-2C08**

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 3730

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

*Types of relevant prior art found:*

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

**Comments:**

**Drop off or send completed forms to STIC/EIC3700 CP2 2C08**



18/9/10 (Item 10 from file: 350)  
DIALOG(R) File 350:Derwent WPIX  
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008989062 \*\*Image available\*\*  
WPI Acc No: 1992-116330/199215  
XRAM Acc No: C92-054131  
XRPX Acc No: N92-086985

**Use of collagenase for treatment of injured nerves - and adhesive formulation contg. collagenase and fibrin for use in surgery**

Patent Assignee: ADVANCE BIOFACTURES CURACAO NV (ADBI-N)

Inventor: WEHLING P

Number of Countries: 007 Number of Patents: 006

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
EP 479615	A	19920408				199215 B
US 5173295	A	19921222	US 90593778	A	19901005	199302
US 5279825	A	19940118	US 90593778	A	19901005	199404
			US 92941570	A	19920908	
EP 479615	B1	19950308	EP 91309137	A	19911004	199514
DE 69107946	E	19950413	DE 607946	A	19911004	199520
			EP 91309137	A	19911004	
ES 2069219	T3	19950501	EP 91309137	A	19911004	199524

Priority Applications (No Type Date): US 90593778 A 19901005

Cited Patents: GB 1251398; US 4524065; US 4645668

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 479615	A		17		
				Designated States (Regional): DE ES FR GB GR IT	
US 5173295	A		14	A61K-037/54	
US 5279825	A		14	A61K-037/54	Div ex application US 90593778 Div ex patent US 5173295
EP 479615	B1 E		18	A61K-038/46	
				Designated States (Regional): DE ES FR GB GR IT	
DE 69107946	E			A61K-038/46	Based on patent EP 479615
ES 2069219	T3			A61K-038/46	Based on patent EP 479615

Abstract (Basic): EP 479615 A

The following are claimed: (A) a method of enhancing the regeneration of injured nerves which comprises supplying collagenase to the zone of injury of the nerve during the regeneration process; (B) an adhesive formulation comprising fibrin or precursor as **adhesive** and **collagenase** to enhance regeneration and rejoining of a severed nerve when the formulation is used as adhesive for the nerve stumps; (C) a pharmaceutical kit for surgical use comprising fibrin **adhesive** or fibrin precursor and **collagenase**; (D) use of collagenase for the mfr. of a medicament for enhancing the regeneration of injured nerves.

USE/ADVANTAGE - Collagenase enhances the nerve regeneration and it can be used with fibrin or a fibrin precursor as an adhesive to repair severed nerves where there is total severence of the nerve trunk or in injury resulting in neuroma in continuity where damage is caused by crushing, bruising or partial laceration of the nerve.

Dwg.1/6

Abstract (Equivalent): EP 479615 B

An adhesive formulation comprising fibrin or a fibrin precursor as **adhesive** and **collagenase** present in an amount and **concentration** effective to enhance regeneration and rejoining of a severed nerve when said formulation is used as adhesive for the stumps.

Dwg.0/6

Abstract (Equivalent): US 5173295 A

John Sims EIC 3700 308-4836

Enhancing the regeneration of injured nerves comprises admin. of collagenase to the injury zone during regeneration. Pref. it is applied in a pharmaceutically acceptable medium, esp. normal saline in an amt. of 200-2,500 esp. 500-1,000 ABC units of collagenase/ ml .

Where the nerve has been severed collagenase is pref. applied to the ends of the proximal and distal stumps. Fibrin contg. collagenase is pref. used as an adhesive for the stumps and the same mixt. used to coat them after suturing.

ADVANTAGE - Growth of nerve sprouts in the injury zone is aided by the presence of collagenase

Dwg.0/6

US 5279825 A

Adhesive formulation comprises fibrin **adhesive** and **collagenase** to enhance regeneration and rejoining of a severed nerve, the formulation being used as an adhesive for the stumps. Pref. 500 - 1500 ABC units of collagenase are present. USE - The compsn can be used when the stubs of severed nerves are to be reunited either directly or by interposition of a nerve graft.

Dwg.0/6

Title Terms: COLLAGENASE; TREAT; INJURY; NERVE; ADHESIVE; FORMULATION;

CONTAIN; COLLAGENASE; FIBRIN; SURGICAL

Derwent Class: B04; D16; P34

International Patent Class (Main): A61K-037/54; A61K-038/46

International Patent Class (Additional): A61K-038/43; A61L-025/00

File Segment: CPI; EngPI

Manual Codes (CPI/A-N): B04-B02C3; B04-B04D2; B12-C10; D05-C03

Chemical Fragment Codes (M1):

\*01\* M423 M431 M782 M903 P942 Q233 V600 V613

\*02\* M423 M431 M782 M903 P942 Q233 V802 V814

?

15/3,KWIC/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

0008170223 BIOSIS NO.: 199293013114

**EFFECTS OF METHYLMERCURIC CHLORIDE ON COLLAGEN INDUCED PLATELET ADHESION  
AND AGGREGATION IN-VITRO**

AUTHOR: KOSTKA B (Reprint); MIELICKI W

AUTHOR ADDRESS: DEP BIOCHEM, INST ENVIRONMENTAL RES AND BIOANALYSIS,  
MEDICAL ACAD, UL MUSZYNSKIEGO 1, 90 151 LODZ, POL\*\*POLAND

JOURNAL: Journal of Trace Elements in Experimental Medicine 4 (3): p  
149-156 1991

ISSN: 0896-548X

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Methylmercuric chloride (MMC) enhances rat platelet **adhesiveness** to **collagen** fibers. Synergic effect between MMC and collagen in platelet aggregation induced by these activators was also observed. The **concentration** of **collagen** required to produce half-maximum aggregation (K') was determined in vitro with the use of platelet-rich plasma obtained from pig blood. K' values for collagen decreased significantly in the presence of very low, nonaggregating concentrations of MMC (0.001-10  $\mu$ M). Such a result indicated that MMC can potentiate platelet responsiveness to collagen.

15/3,KWIC/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0005635888 BIOSIS NO.: 198783114779

**STUDIES OF PLATELET ADHESIVENESS TO COLLAGEN FIBERS I. FUNDAMENTAL  
STUDY OF A TECHNIQUE FOR MEASURING PLATELET ADHESIVENESS TO COLLAGEN  
FIBERS**

AUTHOR: MASE K (Reprint)

AUTHOR ADDRESS: DEP INTERN MED, KANSAI MED UNIV, MORIGUCHI, OSAKA, JAPAN\*\*  
JAPAN

JOURNAL: Journal of the Kansai Medical University 38 (2): p145-159 1986

ISSN: 0022-8400

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: JAPANESE

**STUDIES OF PLATELET ADHESIVENESS TO COLLAGEN FIBERS I. FUNDAMENTAL  
STUDY OF A TECHNIQUE FOR MEASURING PLATELET ADHESIVENESS TO COLLAGEN  
FIBERS**

...ABSTRACT: GBC method), as other available methods using collagen and subendothelium are too complex for clinical use. We have studied a new method of measuring platelet **adhesiveness** to **collagen** fibers supported on sepharose (CS method). The results of fundamental studies on platelet adhesiveness using CS method were as follows: 1. With increasing **collagen concentration**, platelet **adhesiveness** increased. 2. Platelet adhesiveness was not change at a stirring speed of 150 to 15,00 rpm and at a stirring time of over one...

...change in the presence of above 0.5mM EDTA which inhibited platelet aggregation. 4. The influence of the platelet count at 10-40 .times.

104/.  $\mu$ l on the platelet adhesiveness did not observed, but at above 60 .times. 104/.  $\mu$ l, platelet adhesiveness slightly decreased. 5. After storage for 72hr at room tempeature, platelet **adhesiveness** to **collagen** was slightly decreased and markedly decreased (below 50% of control values) after 7 days. 6. Platlets adhered normally to collagen fibers without extracellular von Willebrand...

...is simpler than other methods employing collagen and closer to in vivo conditions than the GBC method. These results suggested that the mechanism of platelet **adhesivness** to **collagen** fibers differ from that of adhesion to glass.

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Hilight option is not available in file(s) 252, 399  
HILIGHT set on as ' '  
? t s10/3,kwic  
>>>KWIC option is not available in file(s): 252, 399

10/3,KWIC/1 (Item 1 from file: 8)  
DIALOG(R)File 8: Ei Compendex(R)  
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05758320 E.I. No: EIP01015485477

**Title: Adhesion strength differential of human ligament fibroblasts to collagen types I and III**

Author: Yang, Li; Tsai, Cliff M.-H.; Hsieh, Adam H.; Lin, Victor S.; Akesson, Wayne H.; Sung, K.-L. Paul

Corporate Source: Univ of California, San Diego, La Jolla, CA, USA

Source: Journal of Orthopaedic Research v 17 n 5 Sep 1999. p 755-762

Publication Year: 1999

CODEN: JOREDR ISSN: 0736-0266

Language: English

...Abstract: used to measure the force required to separate fibroblasts of the anterior cruciate and medial collateral ligaments from substrates composed of type I or III **collagen**, each at a **concentration** of 2 or 5  $\mu\text{g}/\text{mL}$ . Approximately 1,200 fibroblasts from the anterior cruciate ligament and 1,600 from the medial collateral ligament were used, and the adhesion force and area...

...from the anterior cruciate ligament exhibited greater adhesion force than did those from the medial collateral ligament for all concentrations of types I and III **collagen**. In addition, the **adhesiveness** of fibroblasts from both ligaments was dependent on seeding time for all experimental conditions. To determine the adhesiveness per unit area, defined here as the...

? t s10/3,kwic/2

>>>KWIC option is not available in file(s): 252, 399

10/3,KWIC/2 (Item 2 from file: 8)  
DIALOG(R)File 8: Ei Compendex(R)  
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05743055 E.I. No: EIP00125458919

**Title: New type of surgical adhesive made from porcine collagen and polyglutamic acid**

Author: Sekine, Takashi; Nakamura, Tatsuo; Shimizu, Yasuhiko; Ueda, Hiroki; Matsumoto, Kazuya; Takimoto, Yukinobu; Kiyotani, Tetsuya

Corporate Source: Kyoto Univ, Kyoto, Jpn

Source: Journal of Biomedical Materials Research v 54 n 2 Feb 2001. p 305-310

Publication Year: 2001

CODEN: JBMRBG ISSN: 0021-9304

Language: English

**Title: New type of surgical adhesive made from porcine collagen and polyglutamic acid**

...Abstract: tensile strength and histological examination were performed 5, 7, 10, and 14 days after the operation. The tensile strength of wounds treated with 2.5  $\text{mg}/\text{mL}$  **collagen glue** was not significantly different from that of wounds treated with fibrin glue except at 7 days after the operation (p less than 0.05 by Student's t-test). Histological examination revealed that the speed of cell infiltration into, and



absorption of 2.5 mg / mL collagen glue was slower than for fibrin glue, but faster than for 5.0 mg / mL collagen glue . One of the important advantages of our collagen glue is that the absorption rate of it can be controlled by the collagen concentration . Therefore, it seems to be adequate for sealing air leakage from the lung, which takes a relatively long period for recovery. Moreover it does not...

Descriptors: Biomaterials; Adhesives ; Collagen ; Polyesters; Tensile strength

? t sl0/3,kwic/3-10

>>>KWIC option is not available in file(s): 252, 399

10/3,KWIC/3 (Item 1 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2003 Inst for Sci Info. All rts. reserv.

05963148 Genuine Article#: XK721 No. References: 39

**Title: Recombinant human bone morphogenetic protein-2 promotes wound healing in rat periodontal fenestration defects**

Author(s): King GN (REPRINT) ; King N; Cruchley AT; Wozney JM; Hughes FJ  
Corporate Source: ST BARTHOLOMEWS & ROYAL LONDON SCH MED & DENT,FAC CLIN DENT, DEPT PERIODONTOL, TURNER ST/LONDON E1 AD//ENGLAND/ (REPRINT); ST BARTHOLOMEWS & ROYAL LONDON SCH MED & DENT,FAC CLIN DENT, DEPT ORAL PATHOL/LONDON E1 AD//ENGLAND/; GENET INST INC,/CAMBRIDGE//MA/02140

Journal: JOURNAL OF DENTAL RESEARCH, 1997, V76, N8 (AUG), P1460-1470

ISSN: 0022-0345 Publication date: 19970800

Publisher: AMER ASSOC DENTAL RESEARCH, 1619 DUKE ST, ALEXANDRIA, VA 22314

Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

...Abstract: in the mandibles of Wistar rats under general anesthesia. After the root surfaces were acid-conditioned, a 10-mu L quantity of 50 mu g/ mL rhBMP-2 in a collagen gel solution was placed into the surgically created defect in test animals; in controls, either a 10-mu L quantity of only collagen gel was received, or...

...or 38 days after surgery and the tissues processed for histological examination. Transverse 5-mu m sections were stained for the identification of new bone, cementum, and collagen fiber formation. In the 10-day study groups, new bone formation over the second molar and beyond the defect was significantly increased in the test...

10/3,KWIC/4 (Item 2 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
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02665839 Genuine Article#: LU761 No. References: 35

**Title: EFFECT OF FIBRIN SEALANT ON THE INTEGRITY OF COLONIC ANASTOMOSES IN RATS WITH FECAL PERITONITIS**

Author(s): VANDERHAM AC; KORT WJ; WEIJMA IM; VANDENINGH HFGM; JEEKEL H  
Corporate Source: ERASMUS UNIV ROTTERDAM,EXPTL SURG LAB/3000 DR ROTTERDAM//NETHERLANDS/; ST CLARA HOSP,DEPT PATHOL/ROTTERDAM//NETHERLANDS/

Journal: EUROPEAN JOURNAL OF SURGERY, 1993, V159, N8 (AUG), P425-432

ISSN: 1102-4151

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

...Abstract: single layer end-to-end anastomosis fashioned with 7/0 polypropylene. Faecal peritonitis was then induced in half of the rats by placement of 200 mg powdered autoclaved rat faeces in the peritoneal cavity near the anastomosis. Rats were allocated to one of

four groups (n = 30 in each): 1-control...

...additional sealing with fibrin glue; 3-peritonitis alone; and  
4-peritonitis with fibrin glue.

Main outcome measures: Body weight, adhesion formation, anastomotic bursting pressure and **collagen concentration** around the anastomosis on days 2, 4, and 7 in 10 rats from each group.

Results: 11 rats died of peritonitis before the experiment was...

...days 4 and 7, and this was not prevented by fibrin. Sealing of anastomoses resulted in lower bursting pressures on day 4 in control animals. **Collagen concentration** was significantly reduced in peritonitis with or without fibrin sealant on days 4 and 7, and after fibrin sealing of control anastomoses.

Conclusion: Faecal peritonitis reduced mechanical strength and **collagen concentration** of colonic anastomoses, and this was not prevented by additional sealing of the anastomosis with fibrin sealant.  
...Identifiers-- **COLLAGEN** -METABOLISM; **ESCHERICHIA-COLI**; **TISSUE ADHESIVES** ; RESECTION; EXPERIENCE; SURGERY; RECTUM; WOUNDS

10/3,KWIC/5 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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0013667894 BIOSIS NO.: 200200261405

**Expression of GPVI alone confers collagen signaling in RBL-2H3 cells but inactivation of both GPVI and alpha2betal is required to inhibit the collagen response of human platelets**

AUTHOR: Chen Hong (Reprint); Locke Darren (Reprint); Liu Changdong (Reprint); Liu Ying (Reprint); Kahn Mark L (Reprint)

AUTHOR ADDRESS: Molecular Cardiology, University of Pennsylvania, Philadelphia, PA, USA\*\*USA

JOURNAL: Blood 98 (11 Part 1): p786a-787a November 16, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207

SPONSOR: American Society of Hematology

ISSN: 0006-4971

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: developed a monoclonal antibody, 11A12, which blocks calcium signaling in response to collagen but not the GPVI agonist convulxin in RBL-2H3 cells. 30 mug/ **ml** 11A12 had a small inhibitory effect on platelet aggregation induced by low (1 mu/ **ml** ) but not high **concentrations** of **collagen** (10 and 30 mug/ **ml** ). A similar small inhibitory effect was observed with the alpha2betal-blocking antibody 6F1 used at the same concentration. Strikingly, a combination of 11A12 and 6F1 virtually ablated platelet aggregation in response to collagen (30 and 60 mug/ **ml** ). Our results suggest that (1) GPVI is sufficient for both **adhesive** and signaling responses to **collagen** ; (2) GPVI-mediated collagen responses are receptor-density dependent; (3) inhibition of collagen stimulated aggregation of human platelets requires inhibition of both GPVI and alpha2betal...

10/3,KWIC/6 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
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12138457 EMBASE No: 2003249334

**Adhesive properties of hepatoma cells to collagen IV coated surfaces**

Zhao T.; Ling Z.-Q.; Yu W.-Q.; Long M.; Cai S.-X.

Dr. Z.Q. Ling, Zhejiang Academy of Medical Sciences, Hangzhou 310013  
China

AUTHOR EMAIL: lingzq@hotmail.com

Hepatobiliary and Pancreatic Diseases International ( HEPATOBILIARY  
PANCREATIC DIS. INT. ) (China) 2002, 1/4 (565-569)

CODEN: HPDIA ISSN: 1499-3872

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 12

**Adhesive properties of hepatoma cells to collagen IV coated surfaces**

Objectives: To quantitatively study the **adhesive** properties of hepatoma cells to **collagen** IV coated artificial basement membrane and to investigate the relevance of cell **adhesive** forces to the **concentration** of **collagen** IV. Methods: Synchronous G1 and S phase cells were achieved using thymine-2-desoxyriboside and cochinine sequential blockage method and double thymine-2-desoxyriboside blockage...

...60 +/- 107.88) x 10SUP-10N, (298.91 +/- 144.13) x 10SUP-10N when the concentration of the membrane coated by 1, 2, 5 mug/ ml collagen IV respectively (P<0.001). The adhesive forces of G1 and S phases hepatoma cells to artificial basement membrane were (275.86 +/- 232.80 ) x 10SUP-10N and (161.16 +/- 120.40) x 10SUP-10N respectively when the concentration of the membrane coated by 5 mug/ ml collagen IV (P < 0.001). Conclusions: The adhesive forces of hepatoma cells to artifical basement membrane in direct proportion to the **concentration** of **collagen** IV suggests that the increase of basement membrane might be conducive to the chemotactic motion and adhesiveness of tumor cells. G1 phase cells are more...

10/3,KWIC/7 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
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06347261 EMBASE No: 1996009363

**Selective adhesion of hepatocytes on patterned surfaces**

Bhatia S.N.; Toner M.; Tompkins R.G.; Yarmush M.L.

Shriners Burns Institute Res. Center, One Kendall Square, Cambridge, MA  
02139 United States

Annals of the New York Academy of Sciences ( ANN. NEW YORK ACAD. SCI. ) ( United States) 1994, 745/- (187-209)

CODEN: ANYAA ISSN: 0077-8923

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

...hepatocytes on a glass substrate with large regions of adhesive (AS) and nonadhesive (NAS) surfaces was obtained. The AS had hydrophilic characteristics, enhancing deposition of **collagen** molecules from an aqueous **solution**, and subsequent hepatocyte adhesion, whereas the NAS had hydrophobic properties and remained collagen-free and hepatocyte-free. In addition, a reproducible processing technique for obtaining...

...optimized, using a surface with a single AS band as a first approximation to a micropatterned device. This was achieved by spin-coating an aqueous **collagen** type I **solution** (0.1 **mg** / **mL** ) on a banded surface at 500 rpm for 25 seconds. The morphology and long-term function of the hepatocytes attached to AS in nonbanded and...

...and limited to in vivo values. An optimal channel length of 0.6 cm and a flow rate of  $2.0 \times 10^6$  **mL** /s were obtained for a channel of 100  $\mu$ m in width and 10  $\mu$ m in height. These values were reasonable in terms of practical implementation.

DRUG DESCRIPTORS:

**collagen** ; **adhesive agent** ; glass

10/3,KWIC/8 (Item 1 from file: 149)

DIALOG(R)File 149:TGG Health&Wellness DB(SM)

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01797600 SUPPLIER NUMBER: 21195529 (USE FORMAT 7 OR 9 FOR FULL TEXT)

**Regulation of integrin-mediated adhesion by muscarinic acetylcholine receptors and protein kinase C in small cell lung carcinoma.**

Quigley, Robert L.; Shafer, Shulamith H.; Williams, Carol L.

Chest, v114, n3, p839(8)

Sept,

1998

PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0012-3692

LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional

WORD COUNT: 4711 LINE COUNT: 00397

... American Type Culture Collection; Beltsville, Md). Both cell lines were cultured in RPMI-1640 medium, 10% heat inactivated calf bovine serum (CBS), glutamine (0.3 **mg** / **mL** ), penicillin (20 U/ **mL** ), and streptomycin sulfate (20 (micro)g/ **mL** ). Cells were maintained at 37 (degrees) C in a humidified atmosphere of 5% (CO.sub.2)/95% air at densities that promoted exponential proliferation.

Coating of Microtiter Plates With ECM Proteins

Wells of microtiter plates were coated with poly-L-lysine (30 (micro)g/ **mL** phosphate-buffered saline solution (PBS)) or BSA (30 (micro)g/ **mL** PBS) by adding 100 (micro)L of the protein solutions to each well. After incubation for 3 h at 25 (degrees) C, the wells were...

...three times with PBS (200 (micro)L per well) and allowed to air dry. Microtiter wells were coated with collagen type I (100 (micro)g/ **mL** ), collagen type IV (100 (micro)g/ **mL** PBS), laminin (30 (micro)g/ **mL** ), vitronectin (30 (micro)g/ **mL** ), or fibronectin (30 (micro)g/ **mL** ) by adding 20 (micro)L of the protein solutions to each well. After incubation for 3 h at 25 (degrees) C, the wells were washed...SCC-9 cells.

The ability of mAChR to regulate integrin activity was further characterized by examining the carbachol-mediated adhesion of SCC-9 cells to **collagen** type IV. **Concentrations** of carbachol that stimulate adhesion of SCC-9 cells to collagen type IV (Fig 2) are similar to the concentrations of carbachol that inhibit cell...

...antibody (Fig 6, right (C)). However, inhibiting cell-cell adhesion with the HECD antibody diminishes the size of the SCC-9 cell aggregates adhering to collagen type IV, resulting in an **adhesive** response that more closely resembles the response of NCI-H345 cells (Fig 6).

#### DISCUSSION

This study demonstrates that PKC or mAChR activation increases integrin-mediated adhesion of SCLC cells. Activation of mAChR increases the

adhesion of SCC-9 cells to **collagen** type IV. This **adhesive** event is mediated by ((Beta).sub.1)-integrins, because it is abrogated by the AIIB2 antibody that blocks ((Beta).sub.1)-integrin function. Our results...X, et al. Mechanisms of 131 integrin-dependent adherence of granulocytic HL60 to fibronectin. J Leukoc Biol 1995; 57:592-99

(23) Kucik DF, Sustin **ML**, Miller JM, et al. Adhesion-activating phorbol ester increases the mobility of leukocyte integrin LFA-1 in cultured lymphocytes. J Clin Invest 1996; 97: 2139...

10/3,KWIC/9 (Item 2 from file: 149)  
DIALOG(R)File 149:TGG Health&Wellness DB(SM)  
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01309414 SUPPLIER NUMBER: 11628438 (USE FORMAT 7 OR 9 FOR FULL TEXT)

**Collagen shields.**

Mondino, Bartly J.

American Journal of Ophthalmology, v112, n5, p587(4)

Nov 15,

1991

PUBLICATION FORMAT: Magazine/Journal ISSN: 0002-9394 LANGUAGE: English

RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional

WORD COUNT: 1785 LINE COUNT: 00181

... 9, 1990) concerned patients who developed corneal epithelial loss and edema after the application of a collagen shield previously impregnated with both Solu-Medrol (40 **mg** / **ml** of methylprednisolone sodium succinate for injection) and gentamicin sulfate (40 **mg** / **ml** of gentamicin sulfate injection). Mixing of the two drugs produced an aggregate, but it was unclear whether the aggregate damaged the cornea by causing chemical...to treat a glaucoma filter bleb leak. Am. J. Ophthalmol. 107:673, 1989.

[11] Weber, P. A., and Baker, N. D.: The use of cyanoacrylate **adhesive** with a **collagen** shield in leaking filtering blebs. Ophthalmic Surg. 20:284, 1989.

[12] Pollard, D. E., and Kaufman, H. E.: Clinical uses of collagen shields. J. Cataract...

...Arch. Ophthalmol. 106:1605, 1988.

[17] Unterman, S. R., Rootman, D. S., Hill, J. M., Parelman, J. J., Thompson, H. W., and Kaufman, H. E.: **Collagen** shield drug delivery. Therapeutic **concentrations** of tobramycin in the rabbit cornea and aqueous humor. J. Cataract Refract. Surg. 14:500, 1988.

[18] O'Brien, T. P., Sawusch, M. R., Dick...

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          (c) 1997 by Fraunhofer-ILV, Germany  
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 File 441:ESPICOM Pharm&Med DEVICE NEWS 2003/Nov W1

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16/3,KWIC/1 (Item 1 from file: 155)  
DIALOG(R) File 155: MEDLINE(R)  
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10406782 96212792 PMID: 8963722

**Lipoprotein(a) inhibits collagen-induced aggregation of thrombocytes.**

Gries A; Gries M; Wurm H; Kenner T; Ijsseldijk M; Sixma J J; Kostner G M  
Institute of Physiology, Graz, Austria.

Arteriosclerosis, thrombosis, and vascular biology (UNITED STATES) May  
1996, 16 (5) p648-55, ISSN 1079-5642 Journal Code: 9505803

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Lipoprotein(a) [Lp(a)] is known to interact with human platelets in vitro. In the present study the effect of physiological **concentrations** of Lp(a) on platelet aggregation was studied. Freshly prepared gel-filtered platelets from healthy donors were incubated for 30 minutes at 37 degrees C with various **concentrations** of Lp(a); aggregation was triggered with ADP, thrombin, and collagen. Control incubations were performed with Tyrode's solution or LDL. Thrombin- and ADP-triggered...

... were only slightly influenced by Lp(a), but aggregation of platelets stimulated with collagen (4 micrograms/mL) was markedly inhibited. Measurable effects occurred at low **concentrations** (0.05 **mg / mL**) of total Lp(a); at 0.5 **mg / mL**, maximum aggregation of platelets was inhibited by 54 +/- 20%, and the aggregation rate was attenuated by 47 +/- 19% compared with platelets incubated with Tyrode's...

... a) yielded similar results. The effect of Lp(a) on platelet aggregation was accompanied by a significant reduction of serotonin release and TXA2 formation. Higher **concentrations** of collagen (> or = 10 micrograms/mL) caused the inhibitory effect on Lp(a) on collagen-induced aggregation to disappear. In contrast, incubation of platelets with 5 **mg / mL** LDL led to a significant increase of aggregation rate, maximum aggregation, serotonin release, and formation of TXA2 when aggregation was induced with 4 micrograms/mL...

... an adhesion assay using fresh whole blood, which mimics the in vitro situation of vessel injury. Lp(a) reduced platelet adhesion at shear rates of 300 and 1600/s by 22.6% and 11.6%, respectively. In addition, Lp(a) reduced the size of platelet aggregates significantly (up to 63%); this...

Descriptors: **Collagen** --pharmacology--PD; \*Lipoprotein(a)--pharmacology --PD; \*Platelet **Adhesiveness** --drug effects--DE  
? ds



? ds

Set	Items	Description
S1	14412	COLLAGEN?
S2	871749	ADHESIV? OR BONDING? OR GLUE? OR CEMENT?
S3	1261	S1 AND S2
S4	418487	CONCENTRAT?
S5	138	S3 AND S4
S6	227011	MG OR MILLIGRAM?
S7	38	S5 AND S6
S8	424	MILLILITER OR MILLILITRE
S9	146041	ML
S10	146348	S8 OR S9
S11	56	S5 AND S10
S12	66	S7 OR S11
S13	635053	300 OR 400 OR 500 OR 600 OR 700 OR 800
S14	635094	S12 OR S13
S15	25	S12 AND S13
S16	236	S1(4N)S2
S17	16	S4 AND S16
S18	10	S17 AND (S6 OR S10)

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File 371:French Patents 1961-2002/BOPI 200209

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? ds

Set	Items	Description
S1	663968	COLLAGEN?
S2	1110579	ADHESIV? OR GLUE? OR BONDING()AGENT? OR CEMENT?
S3	3527	S1(5N)S2
S4	11989116	CONCENTRATION? OR SOLUTION? OR SOLN
S5	14808	S4(4N)S1
S6	94	S3 AND S5
S7	53	RD (unique items)
S8	3134167	MG OR MILLIGRAM?
S9	1742138	ML OR MILLILITER OR MILLILITRE OR MILLI() (LITRE OR LITER)
S10	9	S7 AND (S8 OR S9)
S11	2415987	MU OR MUG
S12	1837125	S11 NOT (S8 OR S9)
S13	2	S7 AND S12
S14	2	S13 NOT S10
S15	2	RD (unique items)

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Set	Items	Description
S1	83299	COLLAGEN?(S) (ADHESI? OR GLUE? OR ADHERE? OR BOND? OR CEMENT? OR CONGLUTIN? OR AGGLUTIN? OR BIND? OR HOLD?)
S2	128606	MG(1N)ML
S3	7728829	CONCENTRAT?
S4	314	S1(S)S2(S)S3
S5	121	RD (unique items)
S6	3456196	300 OR 400 OR 500 OR 600 OR 700 OR 800
S7	4864	S6(3N)S2
S8	2	S5 AND S7
S9	2	RD (unique items)
S10	314635	ADHESIV?/DE
S11	361173	COLLAGEN?/DE
S12	2677	S10 AND S11
S13	334	S3 AND S12
S14	45	S6 AND S13
S15	40	RD (unique items)
S16	1	S2 AND S15

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FILE 'HCAPLUS, RUSSCI' ENTERED AT 13:55:14 ON 10 NOV 2003

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L3 2461182 S CONCENTRAT? OR SOLUTION? OR SOLN  
L4 585 S L1(5N)L2  
L5 1796 S L1(4N)L3  
L6 24 S L4 AND L5  
L7 23 S L6 AND PY<2002

FILE 'CONFSCI' ENTERED AT 14:03:31 ON 10 NOV 2003

L8 3051 S COLLAGEN?  
L9 4886 S ADHESIV? OR GLUE? OR BONDING OR CEMENT?  
L10 11 S L8 AND L9  
L11 25074 S CONCENTRAT? OR SOLUTION? OR SOLN?  
L12 0 S L10 AND L11  
L13 11 S L10

FILE 'EMA' ENTERED AT 14:08:56 ON 10 NOV 2003

L14 296 S COLLAGEN?  
L15 17382 S ADHESIV? OR GLUE? OR BONDING? OR CEMENT?  
L16 65 S L14 AND L15  
L17 35450 S CONCENTRAT? OR SOLN? OR SOLUTION?  
L18 11 S L16 AND L17  
L19 1954 S MG OR MILLIGRAM? OR MILLI()GRAM?  
L20 1 S L18 AND L19  
L21 452 S ML OR MILLILITER OR MILLILITRE OR MILLI() (LITER OR LITRE)  
L22 0 S L18 AND L21  
L23 10 S L18 NOT L20

=>

PROberts

ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 2001:721611 HCAPLUS  
DOCUMENT NUMBER: 135:243293  
TITLE: Adhesive composition based on natural and synthetic polymers and process for preparing the same  
INVENTOR(S): Bucevski, Mircea Dan; Caloianu, Maria; Colt, Monica; Iordachel, Radu; Iordachel, Catalin  
PATENT ASSIGNEE(S): Institutul National de Cercetare - Dezvoltare pentru Stiinte Biologice, Bucuresti, Rom.  
SOURCE: Rom., 4 pp.  
CODEN: RUXXA3  
DOCUMENT TYPE: Patent  
LANGUAGE: Romanian  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RO 116293	B1	20001229	RO 1997-727	19970415 <--

PRIORITY APPLN. INFO.: RO 1997-727 19970415

AB Transparent adhesives for pharmaceutical products and food packaging contain 80-120 volume parts 5-10% aqueous soln. benzoylated collagen with average mol. weight 40,000-80,000 and benzoyl group content 2-9%, 0.5-1.5 volume parts starch, 0.25-0.75 volume parts polyvinyl alc. (Kw 120, hydrolysis degree 70-90%), 10-20 volume parts acrolein-styrene copolymer (d.p. 200-600), 1-3 volume parts sulfated castor oil, 0.05-0.1 volume part thymol, and 1-5 volume parts 10% aqueous NaOH.

=> d 17 ibib abs 2-23

L7 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 2001:423419 HCAPLUS  
DOCUMENT NUMBER: 135:37219  
TITLE: Polymerization catalysts showing high activity at room temperature in the presence of water and dental polymerizable compositions containing them  
INVENTOR(S): Kimura, Mikio; Aisawa, Masayuki  
PATENT ASSIGNEE(S): Tokuyama Corp., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001158804	A2	20010612	JP 1999-363883	19991222 <--

PRIORITY APPLN. INFO.: JP 1999-270171 A 19990924

AB Title compns., useful as dental adhesives, contain (meth)acrylate-type monomers and the catalysts comprising redox polymerization catalysts, azo compds., and optionally transition metal compds. Pretreated collagen and a soln. containing Me methacrylate, benzoyl peroxide, dimethyl-p-toluidine, and 2,2'-azobis(2,4-dimethylvaleronitrile) were kept at 37° and relative humidity 100% for 1 h to give a polymer with Mn 17,000, Mw 210,000, and graft ratio 16.3%.

L7 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

PROberts

ACCESSION NUMBER: 2000:754415 HCAPLUS  
DOCUMENT NUMBER: 133:325698  
TITLE: Collagen containing tissue adhesive  
INVENTOR(S): Petito, George D.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 32,031,  
abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6136341	A	20001024	US 1999-417911	19991013 <--

PRIORITY APPLN. INFO.: US 1998-32031 B2 19980227

AB A tissue adhesive compound may be a powder, gel, paste or film. The main ingredient is hydrolyzed Type I collagen having a mol. weight between 1000 and 10,000. The collagen is preferably derived from a bovine source, especially calves under one year of age. The gel form preferably includes 60% hydrolyzed Type I collagen, and has anti-microbial properties not found in the powder form. In any form, the compound is administered to the cleaned wound site where it absorbs exudate, provides phys. barrier to bacterial infestation, reduces pain and expedites wound healing. Removal of any compound remaining is unnecessary in subsequent dressing changes.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:475567 HCAPLUS  
DOCUMENT NUMBER: 133:94612  
TITLE: Tissue adhesive for treating vigorously bleeding surfaces comprising collagen and albumin  
INVENTOR(S): Browdie, David A.  
PATENT ASSIGNEE(S): USA  
SOURCE: PCT Int. Appl., 20 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040277	A1	20000713	WO 1999-US504	19990108 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2358567	AA	20000713	CA 1999-2358567	19990108 <--
AU 9923147	A1	20000724	AU 1999-23147	19990108 <--
EP 1140233	A1	20011010	EP 1999-903029	19990108 <--



PROberts

R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE, FI  
PRIORITY APPLN. INFO.: WO 1999-US504 A 19990108

AB Disclosed is a novel tissue adhesive technol. comprising a combination of ultrasonically treated proteins including collagen and albumin which form a viscous material that develops adhesive properties when chemical crosslinked. A novel new crosslinking agent with surprisingly stable properties was developed in association with the tissue adhesive described and claimed herein and is considered to be within the scope of the present invention. This new crosslinking agent is a product of reaction glutaraldehyde with amino acids or peptides and allowing the reacting to proceed to completion. This chemical crosslinking is mixed with the ultrasonically treated proteins, allowed to react for a predetd. time, then used to seal large surface areas of vigorously bleeding tissues including, but not limited to, the liver, lungs and major vascular systems in patients with and without bleeding disorders. This same tissue adhesive has proven to work well in sealing suture sites to prevent leakage. Four to eight parts of collagen/albumin soln . was mixed with one part of glutaraldehyde solution and 0.01% methylene blue to make the tissue adhesive of the invention. Efficacy of the tissue adhesive was shown in vivo.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:630306 HCAPLUS

DOCUMENT NUMBER: 131:248293

TITLE: Method for making mineralized collagen fibrils and their use as bone replacement material

INVENTOR(S): Weis, Karl; Pompe, Wolfgang; Bradt, Jens

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Eur. Pat. Appl., 4 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 945147	A2	19990929	EP 1999-105435	19990317 <--
EP 945147	A3	20000503		
EP 945147	B1	20030827		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19812713	A1	19990930	DE 1998-19812713	19980324 <--
AT 247993	E	20030915	AT 1999-105435	19990317
JP 11313882	A2	19991116	JP 1999-77490	19990323 <--
US 6384196	B1	20020507	US 1999-275397	19990324

PRIORITY APPLN. INFO.: DE 1998-19812713 A 19980324

AB Mineralized collagen fibrils are produced in a single step by mixing an acidic soln. of soluble recombinant collagen with a neutral buffer soln. while adding a Ca solution and a phosphate solution to produce a supersatd. Ca phosphate solution under controlled conditions such that fibril formation begins before mineralization but is limited to the extent that Ca and phosphate ions can diffuse into the collagen fibrils. The mineralized fibrils are then used in preparation of a composite Ca phosphate cement containing embedded fibrils for use as a bone substitute. Thus, 700 µL of a soln. of soluble type I collagen (1 mg/mL) in 10 mM HCl was mixed with 126 µL 0.1M aqueous

PROberts

CaCl<sub>2</sub> soln. at 4° (component 1). Component 2 comprised a mixt. of 165 µL 2M aq. NaCl soln., 240 µL 0.5M aq. Tris buffer (pH 7.4), 32.4 µL 0.5M aq. KH<sub>2</sub>PO<sub>4</sub>/K<sub>2</sub>HPO<sub>4</sub> soln. (pH 7.4), and 793 µL H<sub>2</sub>O at 4°. Component 2 (574 µL) was added to component 1 and the temp. was rapidly raised to 30° to initiate fibril formation and mineralization. The amorphous Ca phosphate phase which formed initially was converted over the next 90 min to cryst. defect apatite which was deposited on the fibrils. The product, which had the consistency of a gel, was washed in distd. water to remove buffering salts and freeze-dried. These mineralized fibrils (5 mg) were combined with 500 mg Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub>/CaCO<sub>3</sub> mixt. and 230 mL phosphate buffer to form a plastic cement mass which subsequently hardened.

L7 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:630305 HCAPLUS

DOCUMENT NUMBER: 131:248292

TITLE: Method for making mineralized collagen fibrils and their use as bone replacement material

INVENTOR(S): Weis, Karl; Pompe, Wolfgang; Bradt, Jens

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Eur. Pat. Appl., 4 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 945146	A2	19990929	EP 1999-105434	19990317 <--
EP 945146	A3	20000426		
EP 945146	B1	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19812714	A1	19990930	DE 1998-19812714	19980324 <--
AT 240128	E	20030515	AT 1999-105434	19990317
JP 11313883	A2	19991116	JP 1999-77494	19990323 <--
US 6384197	B1	20020507	US 1999-275398	19990324
PRIORITY APPLN. INFO.:		DE 1998-19812714 A 19980324		

AB Mineralized collagen fibrils are produced in a single step by mixing an acidic soln. of soluble recombinant collagen with a neutral buffer soln. while adding a Ca solution and a phosphate solution to produce a supersatd. Ca phosphate solution under controlled conditions such that fibril formation begins before mineralization but is limited to the extent that Ca and phosphate ions can diffuse into the collagen fibrils. The mineralized fibrils are then used in preparation of a composite Ca phosphate cement containing embedded fibrils for use as a bone substitute. Thus, 700 µL of a soln. of soluble type I collagen (1 mg/mL) in 10 mM HCl was mixed with 126 µL 0.1M aqueous CaCl<sub>2</sub> soln. at 4° (component 1). Component 2 comprised a mixt. of 165 µL 2M aq. NaCl soln., 240 µL 0.5M aq. Tris buffer (pH 7.4), 32.4 µL 0.5M aq. KH<sub>2</sub>PO<sub>4</sub>/K<sub>2</sub>HPO<sub>4</sub> soln. (pH 7.4), 37.5 µL aq. Na poly-L-aspartate soln. (4 mg/mL), and 755 µL H<sub>2</sub>O at 4°. Component 2 (574 µL) was added to component 1 and the temp. was rapidly raised to 30° to initiate fibril formation and mineralization. The amorphous Ca phosphate phase which formed initially was converted over the next 8 h to cryst. defect apatite which was deposited on the fibrils. The product, which had the consistency of a gel, was washed in distd. water to remove buffering salts and freeze-dried. These mineralized fibrils (288

Proberts

mg) were combined with 1 g Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub>/CaCO<sub>3</sub> mixt. and stirred with water to form a plastic cement mass which subsequently hardened.

L7 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:510503 HCAPLUS

DOCUMENT NUMBER: 131:175034

TITLE: Pore and structure formation in collagen-hydroxyapatite precursors. Experiment-model

AUTHOR(S): Lampenscherf, S.; Weis, K.; Pompe, W.

CORPORATE SOURCE: Department Materials Science, Technical Univ. Dresden, Dresden, D-01069, Germany

SOURCE: Materials Science Forum (1999), 308-311(Functionally Graded Materials 1998), 362-367  
CODEN: MSFOEP; ISSN: 0255-5476

PUBLISHER: Trans Tech Publications Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The formation was studied of collagen/hydroxyapatite (HAP)-composites with graded porosity. Pore growth was shown during phase separation of an aqueous collagen soln. The influence was investigated of different mech. boundary conditions (freestanding body, film on rigid substrate). The formation is presented of a graded pore structure via phase separation together with the synthesis of a collagen/HAP-composite via a cementation reaction from a colloidal HAP-precursor. The modeling part focuses on the drying process as a route for graded densification and structure formation. The model is described for stress formation and plastic deformation in a 2-phase material containing a liquid and a solid phase. Important processing and material parameters are outlined for structural design and usage of the model to find the optimum processing conditions for a desired graded structure.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:548569 HCAPLUS

DOCUMENT NUMBER: 129:180187

TITLE: Collagenic material useful in particular for preventing post-operative adhesions

INVENTOR(S): Tayot, Jean-Louis; Tardy, Michel; Gravagna, Philippe

PATENT ASSIGNEE(S): Societe Anonyme De Developpement Des Utilisations, Fr.

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834656	A1	19980813	WO 1998-FR214	19980205 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
FR 2759083	A1	19980807	FR 1997-1373	19970206 <--

John Sims EIC 3700 308-4836

PROberts

FR 2759083	B1	19990430		
FR 2759084	A1	19980807	FR 1997-11589	19970917 <--
FR 2759084	B1	19991029		
AU 9862984	A1	19980826	AU 1998-62984	19980205 <--
EP 964709	A1	19991222	EP 1998-906979	19980205 <--
EP 964709	B1	20020502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, LI, FI				
JP 2000509632	T2	20000802	JP 1998-533876	19980205 <--
JP 3231793	B2	20011126		
AT 216897	E	20020515	AT 1998-906979	19980205
ES 2174419	T3	20021101	ES 1998-906979	19980205
US 2001008930	A1	20010719	US 1999-355842	19990805 <--
US 6391939	B2	20020521		

PRIORITY APPLN. INFO.:

FR 1997-1373	A	19970206
FR 1997-11589	A	19970917
WO 1998-FR214	W	19980205

AB A non-toxic, biol. compatible collagenic material, biodegradable in less than a month, preferably in less than a week, comprising collagen and at least a macromol. hydrophilic additive, chemical non-reactive with collagen, said collagen having at least lost its helicoid structure and being cross-linked. The invention also concerns a method for obtaining such a material. The collagenic material is particularly useful for the prevention of post-operative adhesions. A soln. of collagen oxidized by periodic acid in acetone was sterile filtered at 40°. The solution was mixed with PEG-6000 and glycerin and the volume was adjusted to obtain a concn. of 2.7% collagen, 9.0% PEG-6000, and 0.54% glycerin. The mixture was poured on a PVC surface at 0.133 g/cm<sup>2</sup> and left under stream of sterile air for 18 h to evaporate the solvents. The film thus obtained had post-operation antiadherence properties in rats.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:535467 HCAPLUS

DOCUMENT NUMBER: 129:153285

TITLE: Medical hardenable compositions containing collagens and their manufacture

INVENTOR(S): Ishikawa, Kunio

PATENT ASSIGNEE(S): Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10216219	A2	19980818	JP 1997-33221	19970131 <--

PRIORITY APPLN. INFO.: JP 1997-33221 19970131

AB The compns., useful for restoring defects and filling cavities of bone and tooth, and stopping bleeding from lesions in such hard tissues, contain phosphate components and Ca components, collagens or their derivs., and water-soluble phosphate salts in the powder and/or liquid. The whole of these components are dissolved in a liquid to show PO-4 concentration  $\geq 50$  mmol. The compns. provide cement which show good mech. strength, moisture-resistance, biocompatibility, and affinity to bone. A 1:1 mixture of anhydrous CaHPO<sub>4</sub> and tetracalcium phosphate as kneaded with an aqueous neutral

PRoberts

sodium hydrogen phosphate **soln.** containing **collagen** to give a **cement**, which was soaked in H2O to show no decay.

L7 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:514151 HCAPLUS

DOCUMENT NUMBER: 127:145602

TITLE: Recombinant human bone morphogenetic protein-2 promotes wound healing in rat periodontal fenestration defects

AUTHOR(S): King, G.N.; King, N.; Cruchley, A.T.; Wozney, J.M.; Hughes, F.J.

CORPORATE SOURCE: Department of Periodontology, St Bartholomew's & The Royal London School of Medicine & Dentistry, Faculty of Clinical Dentistry, London, E1 AD, UK

SOURCE: Journal of Dental Research (1997), 76(8), 1460-1470

CODEN: JDREAF; ISSN: 0022-0345

PUBLISHER: International Association for Dental Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although there is considerable interest in the use of bone morphogenetic protein (BMP) to promote periodontal regeneration, little is known of its effects on the early stages of wound healing. The aim of this study was to investigate the effects of recombinant human bone morphogenetic protein 2 (rhBMP-2) on an early stage of post-operative wound healing and following complete healing (10 and 38 days, resp.) in a rat model of periodontal regeneration. The buccal aspects of molar roots were carefully denuded of their periodontal ligament through a bony window created in the mandibles of Wistar rats under general anesthesia. After the root surfaces were acid-conditioned, a 10- $\mu$ L quantity of 50  $\mu$ g/mL rhBMP-2 in a **collagen** gel **soln.** was placed into the surgically created defect in test animals; in controls, either a 10- $\mu$ L quantity of only collagen gel was received, or the defect was untreated. Animals were killed 10 days or 38 days after surgery and the tissues processed for histol. examination. Transverse 5- $\mu$ m sections were stained for the identification of new bone, **cementum**, and **collagen** fiber formation. In the 10-day study groups, new bone formation over the second molar and beyond the defect was significantly increased in the test group, although there was no evidence of increased ankylosis. RhBMP-2 stimulated more than twice the area of cementum growth coronally compared with controls (712  $\mu$ M2 and 258  $\mu$ M2, resp.). Connective tissue attachment, including the number and width of collagen bundles, was similar in both test and controls. Complete healing without any evidence of ankylosis had occurred in all animals 38 days post-operatively, and no significant differences were observed between test and control groups. In conclusion, a single dose of rhBMP-2 increased the rate of normal intramembranous bone formation and selectively enhanced cementum formation coronally during early wound healing. However, the finding that rhBMP-2 induced bone formation at some distance from the defect suggests the importance of developing a suitable delivery system to maintain the concentration of BMP-2 at the site of implantation for potential therapeutic use.

L7 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:90184 HCAPLUS

DOCUMENT NUMBER: 124:211912

TITLE: Fibrin-**collagen** composite tissue **adhesive**

AUTHOR(S): Sierra, David H.

Proberts

CORPORATE SOURCE: Cohesion Corp., Palo Alto, CA, USA  
SOURCE: Surgical Adhesives and Sealants (1996),  
29-39. Editor(s): Sierra, David H.; Saltz, Renato.  
Technomic: Lancaster, Pa.  
CODEN: 62KIAS

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The fibrin-based tissue adhesive composition was formulated by adding fibrillar type I collagen to fibrin-factor XIII soln. It appears that addition of collagen to a fibrin sealant alter the sealant's biol., biochem. and mech. properties. The addition of collagen or antifibrinolytic (thrombin) to fibrin sealant did not decrease the onset of degradation. However, the addition of both collagen and antifibrinolytic (thrombin) significantly decreased the onset of degradation in a synergistic manner.

L7 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:761801 HCAPLUS

DOCUMENT NUMBER: 123:152998

TITLE: Adhesive composition for surgical use based on non-crosslinked collagen modified by oxidative degradation

INVENTOR(S): Tardy, Michel; Tiollier, Jerome; Tayot, Jean-louis

PATENT ASSIGNEE(S): Imedex, Fr.

SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 664132	A1	19950726	EP 1995-400093	19950118 <--
EP 664132	B1	20000705		
FR 2715309	A1	19950728	FR 1994-715	19940124 <--
FR 2715309	B1	19960802		
AT 194295	E	20000715	AT 1995-400093	19950118 <--
ES 2149932	T3	20001116	ES 1995-400093	19950118 <--
US 5618551	A	19970408	US 1995-376185	19950120 <--
CA 2140835	AA	19950725	CA 1995-2140835	19950123 <--
CA 2140835	C	20011120		
BR 9500284	A	19951017	BR 1995-284	19950123 <--
AU 9511334	A1	19950803	AU 1995-11334	19950124 <--
AU 692496	B2	19980611		
JP 08033700	A2	19960206	JP 1995-27455	19950124 <--

PRIORITY APPLN. INFO.: FR 1994-715 A 19940124

AB A biocompatible, bioresorbable and non-toxic composition for tissue adhesion comprises a solution of 5-30% non-crosslinked collagen or gelatin modified by oxidative degradation. Bovine collagen 20 g was dissolved in 20 L 0.012N HCl at 4-8° for 8 h, then it was sterile filtered. A solution of 240 g/L NaCl (4.1 L) was added to above collagen soln. and stirred and left for ≥8 h, then it was centrifuged for 15 at 8000 rpm for 15 min. The precipitate was separated and dissolved in 0.012N HCl at a concentration of 0.5% and stirred for ≥8 h at 4-8° followed by addition of 80 mL sterile 0.4M periodic acid at 20° and 0.8 L sterile NaCl (240g/L), then centrifuged at 20° for 15 min at 8500 rpm. The precipitate was separated, washed with NaCl solution and acetone and kept at -80°. Thus, 275 µL of a solution of 0.41M Na2CO3 (1 g) was added

PROberts

to a 15% soln. of above collagen in water at  
42° and mixed for 15 s. After 2.5 min a solid gel was formed.

L7 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 1995:748898 HCAPLUS  
DOCUMENT NUMBER: 123:116202  
TITLE: Process for concentrating biocolloids  
INVENTOR(S): Bian, Baigui; Qiu, Shouchang; Wang, Yanru  
PATENT ASSIGNEE(S): Nanjing College of Chemical Engineering, Peop. Rep.  
China  
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 4 pp.  
CODEN: CNXXEV  
DOCUMENT TYPE: Patent  
LANGUAGE: Chinese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
CN 1098127	A	19950201	CN 1993-111589	19930726 <--
PRIORITY APPLN. INFO.:			CN 1993-111589	19930726
AB	The title process consists of treating biocolloid solution (e.g., 0.1-10% soln. of collagens, glues, gelatins, seaweed glues, pectin) with a semipermeable membrane (e.g., of plastics, inorg.) to give a 15-50% concentration			

L7 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 1993:634131 HCAPLUS  
DOCUMENT NUMBER: 119:234131  
TITLE: Medical adhesives containing fibrinogens and  
collagens  
INVENTOR(S): Iwatsuki, Makoto; Hayashi, Toshiro  
PATENT ASSIGNEE(S): Ajinomoto Kk, Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
JP 05208042	A2	19930820	JP 1992-15139	19920130 <--
PRIORITY APPLN. INFO.:			JP 1992-15139	19920130
AB	A mixture of human fibrinogens and collagens is used as adhesive for skin and during surgery. For example, a fibrinogen soln. and a collagen soln. were mixed and applied on a collagen membrane, then a CaCl2 soln. was applied for gelation and its adhesion strength was determined			

L7 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 1993:109819 HCAPLUS  
DOCUMENT NUMBER: 118:109819  
TITLE: Surgical tissue adhesives  
INVENTOR(S): Tamada, Yasushi; Yasuda, Kenji  
PATENT ASSIGNEE(S): Japan Synthetic Rubber Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent

Proberts

LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04347162	A2	19921202	JP 1991-118559	19910523 <--

PRIORITY APPLN. INFO.: JP 1991-118559 19910523

AB A tissue adhesive contains (1) an oligopeptide containing  $\geq 1$  residue of glutamine and lysine and (2) collagen and/or gelatin. An oligopeptide with 18 amino acid residues in a chain in combination with an aqueous **collagen soln.** was effective in covering wounds in surgery.

L7 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 1992:658275 HCAPLUS  
DOCUMENT NUMBER: 117:258275  
TITLE: **Collagen-based adhesives** and sealants for medical use and methods of preparation thereof  
INVENTOR(S): Kelman, Charles D.; Devore, Dale P.  
PATENT ASSIGNEE(S): Autogenesis Technologies, Inc., USA  
SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9213025	A1	19920806	WO 1992-US704	19920127 <--
W: BR, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5219895	A	19930615	US 1991-646944	19910129 <--
CA 2101637	AA	19920730	CA 1992-2101637	19920127 <--
CA 2101637	C	20030819		
EP 569551	A1	19931118	EP 1992-907406	19920127 <--
EP 569551	B1	20021030		
R: CH, DE, FR, GB, IT, LI				
US 5874537	A	19990223	US 1996-610853	19960305 <--

PRIORITY APPLN. INFO.: US 1991-646944 A 19910129  
WO 1992-US704 W 19920127  
US 1993-31665 A3 19930315  
US 1994-321095 B1 19941007

AB Soluble or partially fibrillar **collagen** monomers in **soln.** are chemical modified, prior to polymerization, with an acylating agent, sulfonating agent or combination of both. The collagen compns. can be used as medical adhesives for bonding soft tissues or be made into a sealant film for a variety of medical uses such as wound closures, tendon wraps, or preventing adhesion formation following surgery. Pure acid soluble collagen (preparation is given) was reacted with anthraquinone-1,5-disulfonic acid and glutaric anhydride, and the modified collagen was separated. Two sections of bovine corium was placed in the above modified **collagen soln.** in phosphate buffer and Na persulfate was added and exposed to UV irradiation for 30 s to bound two sections together which appeared to resist substantial forces.



Proberts

L7 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:598599 HCAPLUS  
DOCUMENT NUMBER: 117:198599  
TITLE: A biologically derived medical **adhesive** containing **collagen** or gelatin and its uses  
INVENTOR(S): Bowyer, Barry L.; Robin, Jeffrey; Terry, Richard N.; Garg, Atul K.  
PATENT ASSIGNEE(S): Bausch and Lomb Inc., USA  
SOURCE: PCT Int. Appl., 31 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9213578	A1	19920820	WO 1991-US9638	19911219 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MW, NO, PL, RO, SD, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2103728	AA	19920812	CA 1991-2103728	19911219 <--
AU 9212498	A1	19920907	AU 1992-12498	19911219 <--
AU 652808	B2	19940908		
EP 563331	A1	19931006	EP 1992-904917	19911219 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
NO 9302838	A	19930810	NO 1993-2838	19930810 <--
PRIORITY APPLN. INFO.:			US 1991-653602	19910211
			WO 1991-US9638	19911219

AB An adhesive composition suited for surgical applications comprises an aqueous **soln.** of **collagen** or gelatin which has a melt index temperature of 33-60° achieved by mixing blends of thermally crosslinked and non-crosslinked biopolymers. The adhesive also contains an antibiotic. A portion of 10% by weight porcine scleral collagen was dried and heated to 145° for 60 min to produce densely crosslinked material. A sec. portion was similarly treated for 15 min at 145° and served as a noncrosslinked sample. A mixture comprising 5% of noncrosslinked and 95% crosslinked material was diluted to various solid concns. (12.5, 15, 20, and 30% collagen) to obtain compns. with different bonding strengths.

L7 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:136326 HCAPLUS  
DOCUMENT NUMBER: 116:136326  
TITLE: A **collagen** medical **adhesive** and its uses  
INVENTOR(S): Bowyer, Barry L.; Robin, Jeffrey  
PATENT ASSIGNEE(S): Bausch and Lomb Inc., USA  
SOURCE: Eur. Pat. Appl., 10 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 466383	A1	19920115	EP 1991-306000	19910702 <--
R: DE, DK, ES, FR, GB, IT, SE				

PRoberts

JP 04231961	A2	19920820	JP 1991-164882	19910705 <--
AU 9180281	A1	19920109	AU 1991-80281	19910708 <--
AU 641254	B2	19930916		
NO 9102664	A	19920110	NO 1991-2664	19910708 <--

PRIORITY APPLN. INFO.: US 1990-549797 19900709

AB A medical adhesive useful in closing wounds and surgical incisions comprises an aqueous **soln.** of **collagen** which has a melt index of 35-45°. Crosslinked and noncrosslinked **collagens** are blended to provide an **adhesive** with a given viscosity, adhesiveness, melt index temperature, setting temperature and transparency.

Thus, a portion of a 35 % **soln.** of naturally occurring **collagen** from a porcine sclera source was dried and heated to 145° for 60 min to produce densely crosslinked collagens and a second portion was similarly treated for 15 min at 145° to serve as a relatively noncrosslinked collagens. A mixture comprising 5 % of the noncrosslinked material and 95 % of the densely crosslinked material was made and diluted to obtain 12.5 % total collagen concentration Rabbit corneal tissue samples were successfully bonded using the composition

L7 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1989:445213 HCAPLUS

DOCUMENT NUMBER: 111:45213

TITLE: Osteoinductivity of carbonate apatite-collagen composites

AUTHOR(S): Ohmae, H.; Okazaki, M.; Hino, T.

CORPORATE SOURCE: Fac. Dent., Osaka Univ., Osaka, 565, Japan

SOURCE: Jinko Zoki (1989), 18(1), 80-3

CODEN: JNZKA7; ISSN: 0300-0818

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB CO3 apatites with chemical compns. and crystallog. properties similar to those of bone was mixed with 0.5 wt% **collagen soln.**

The composites after 4 h-UV-irradiation, and incubation in 0.9% NaCl solution at

37° were less deformed than non-UV-irradiated samples, under a compressive force. The biocompatibility of the composites with surrounding tissues seemed to be good, in the periosteum cranii of rats and rabbits. The composites treated with fibrin glue in addition to the UV-irradiation kept their shape even after 1-mo-implantation. The newly synthesized bone-like substance was observed on the bone facing to the composite.

L7 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1984:39652 HCAPLUS

DOCUMENT NUMBER: 100:39652

TITLE: Tissue-adhering collagen wound dressing

INVENTOR(S): Stemberger, Axel

PATENT ASSIGNEE(S): Ruhland, Dr., Nachfolger G.m.b.H., Fed. Rep. Ger.

SOURCE: Ger., 13 pp.

CODEN: GWXXAW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PROberts

DE 3212412	A1	19831013	DE 1982-3212412	19820402 <--
DE 3212412	C2	19860102		
EP 90997	A2	19831012	EP 1983-102773	19830321 <--
EP 90997	A3	19851030		
EP 90997	B1	19891018		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 47317	E	19891115	AT 1983-102773	19830321 <--
JP 58185162	A2	19831028	JP 1983-58557	19830402 <--
JP 02060339	B4	19901217		

PRIORITY APPLN. INFO.: DE 1982-3212412 19820402  
EP 1983-102773 19830321

AB Wound coverings consist of a 0.3-2-cm-thick layer of collagen coated on 1 or both sides with a 0.2-2-mm-thick fibrinogen layer containing 0.5-10 mg/cm<sup>2</sup>. The fibrinogen contains SH groups derived from sulphydration or reduction of disulfide bridges. The collagen is highly pure (N/hydroxyproline ratio by weight of <3). At least 1 of the layers may contain an antibiotic, antifibrinolytic, and/or thrombin [9002-04-4]. Collagen was prepared from beef tendons by extracting with pH 3.7 citrate buffer, dialyzing against 1% HOAc, incubating at 10° with pepsin at a collagen/pepsin ratio of 50:1, dialyzing against alkaline H<sub>2</sub>O at pH 8, centrifuging, dissolving in 1% HOAc, and dialyzing again until the N/hydroxyproline ratio was <3. A 1.5% **collagen soln.** was prepared in 0.05% HOAc, and 100 mL was poured in a 10 cm + 10 cm form and freeze-dried to give a sponge. Before formation of the sponge, 0.4 g tranexamic acid [1197-18-8], 80,000 units of aprotinin [9087-70-1] or 200 mg gentamycin sulfate [1405-41-0] may be added to the solution. Fibrinogen was dissolved in isotonic saline and incubated at pH 10.6 and 0° for 35 min with N-acetylhomocysteine thiolactone; the reaction was stopped by addition of pH 7 phosphate buffer, and the SH-modified fibrinogen was desalted and concentrated by ultrafiltration.

The **soln.** was sprayed on the **collagen** sponge at 5 mg fibrinogen/cm<sup>2</sup>, and the sponge was freeze-dried and packaged. The collagen layer was 10 cm thick and the fibrinogen layer was .apprx.0.3 mm thick. Results with the use of the gentamycin-containing product in surgical wound healing and hemostasis are described.

L7 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1978:448854 HCAPLUS  
DOCUMENT NUMBER: 89:48854  
TITLE: Fibrinogen **concentrate** and **collagen** sponge as a tissue **adhesive**.

AUTHOR(S): Characterization of adhesion and the adhesive  
Stemberger, A.; Fritsche, H. M.; Bluemel, G.  
CORPORATE SOURCE: Inst. Exp. Chir., Tech. Univ. Muenchen, Munich, Fed. Rep. Ger.

SOURCE: Medizinische Welt (1978), 29(17), 720-4  
CODEN: MEWEAC; ISSN: 0025-8512

DOCUMENT TYPE: Journal

LANGUAGE: German

AB Fibrinkleber, a com. fibrinogen concentrate showed some decrease in the stability after freezing and thawing. Tachotop and Kollagenvlies Pentapharm, collagen sponges, stopped hemorrhaging, but not as well as native collagen. The tensile strengths of both wet and dry Kollagenvlies and Tachotop were less than that of aldehyde-crosslinked collagen sponge.

L7 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1972:512622 HCAPLUS

DOCUMENT NUMBER: 77:112622

TITLE: Effect of temperature, cooking time, and common salt

PROberts

concentration on the solubility of  
collagen in pork muscle solubility of collagen  
in pork muscle

AUTHOR(S): Kopp, J.; Bonnet, Madeleine  
CORPORATE SOURCE: Stn. Rech. Viande, Cent. Rech. Zootech. Veet.,  
Theix/Saint-Genes-Champanelle, Fr.  
SOURCE: Fleischwirtschaft (1971), 51(11), 1647-51  
CODEN: FLEIA8; ISSN: 0015-363X  
DOCUMENT TYPE: Journal  
LANGUAGE: German

AB The epimysial collagen from longissimus dorsi of the pig was extracted and obtained without denaturation. The epimysia was solubilized in HOAc/NaOAc buffer by heating for 1, 3, 6, 10, or 16 hr at 45, 55, 65, and 75° with 0, 5, 10, 15, 20, and 25% NaCl. Hydroxyproline levels were determined and the distribution of different mol. wts. of the protein were found by gel electrophoresis. The solubility of the collagen was highest (80%) at pH 5.00 and 3 hr heating at 55° without NaCl. With 10-15% salt the temperature had to be raised to 65° to achieve the same solubility. Above 15% NaCl concns. even raising the temperature could not produce the same solubility. At

low temps., the solubility increased with heating time but at temps. >65° there was no increase after 1 hr. As soon as the NaCl concentrate exceeded 15% the production of the polymers with mol. weight 300,000 dropped from 50% to low levels, e.g. 5% with 25% salt. Since ham is normally cooked at 65° and these polymers are essential in the renaturation of collagen to cement the meat together and make it firm, it is necessary for good consistency quality to control carefully the modern method of injecting salt. 22 refs.

L7 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1963:4102 HCAPLUS

DOCUMENT NUMBER: 58:4102

ORIGINAL REFERENCE NO.: 58:687f-h

TITLE: The products of dissolution of collagen in  
buffer solutions. II

AUTHOR(S): Shestakova, I. S.; Babloyan, O. O.; Romanov, Yu. A.

SOURCE: Nauchn. Tr. Mosk. Tekhnol. Inst. Legkoj Prom. (1961), (No. 19), 11-18  
From: Ref. Zh., Khim. 1962, Abstr. No. 11P627.

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. ibid. 3-10. A study was made of 9 variants of acid dissoln. of collagen. Untreated raw material was dissolved along with the hair and the epidermis and delimed skin obtained by a unique procedure for the production of leather for shoe soles was dissolved. Collagen was dissolved in buffer solns. at 60° and pH 4 and 2.2. The dissoln. products of collagen were analyzed before and after dialysis. Detns. were made of total N by the Kjeldahl method, of amino N by the Van Slyke method, of hydroxyproline, of dry residue, and of viscosity. Also, color reactions and pptns. with NaCl and EtOH were conducted, and films were obtained and tested. The best conditions for dissoln. of collagen are heating in buffer solns. at 60° for 20-4 hrs. (without draining at pH 4 and with draining at pH 2.2). These conditions may serve as a basis for the production of tech. gelatin and glue. It was possible to obtain these products directly from the raw material, to obtain films from undialyzed solns. of collagen and to use the solns. obtained for application of coatings to chrome-tanned leather dyed by a drum method and for obtaining fibrous material from solns. by precipitation with NaCl. The presence of hydroxyproline in several solns. indicates that coarse parts

PRoberts

of the collagen structure rather than fine fragments go into solution  
Greater destruction of the mol. chains of collagen takes place at pH 2.2  
than at pH 4.

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PRoberts

ANSWER 9 OF 11 CONFSCI COPYRIGHT 2003 CSA on STN

AN 86:42042 CONFSCI

DN 86069827

TI **Collagen**-based calcified tissue **adhesive**

AU Kaleem, K.; Chertok, F.; Erhan, S.

CS Albert Einstein Med. Cent., Philadelphia, PA, USA

SO IADR, 1111 Fourteenth Street, N.W., Suite 1000, Washington, DC 20005  
(USA), Abstract No. 1099.

Meeting Info.: 862 0206: International Association for Dental Research  
64th Annual Meeting (8620206). The Hague (Netherlands). 26-28 Jun 1986.  
International Association for Dental Research (IADR).

DT Conference

FS DCCP

LA UNAVAILABLE

CC 3500 CLINICAL MEDICINE

PROberts

ANSWER 1 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2003(11):C4-Z-918 EMA  
TI Evaluation of ligand binding to type 1 **collagen** through computational and analytical methods.  
AU Vaidyanathan, J. (University of Medicine and Dentistry (New Jersey)); Vaidyanathan, T.K. (University of Medicine and); Ravichandran, S. (University of Medicine and Dentistry (New Jersey)); Klein, B. (University of Medicine and Dentistry (New Jersey))  
SO Switzerland. 2003 Photomicrographs, Graphs, 15 ref.. p. 3061-3066  
Conference: THERMEC 2003: International Conference on Processing & Manufacturing of Advanced Materials, Madrid, Spain, 7-11 Jul 2003  
DT Conference Article; Journal  
CY Switzerland  
LA English  
AB Type 1 **collagen** is a critical component of tissue architecture in the body. Molecular interactions involving **collagen** and **adhesives** used for tissue repair are of critical interest in biomaterials. This was approached using computational and analytical methods in this study. In the computational approach, energy optimized 3-D model structures of type 1 **collagen** and ligands were computer modeled and interactions of low energy conformations of ligands with a **collagen** receptor were evaluated by molecular mechanics computations using a 'random walk' model of the ligand within an interaction zone defined by a box around the static receptor. Binding assays were performed using an immunochemical method in which the binding interactions of a type 1 **collagen** antibody with the **collagen** structure were determined after prior exposure to a solvent containing no ligand (control) and predetermined **concentrations** of the ligand. In addition, modulated DSC scans were used to characterize differences in endotherms associated with potential **collagen**-ligand interactions. Visualization of low energy ligand-**collagen** complexes revealed that the cavities associated with the triple-helical folding of **collagen** fibril structure provided favored sites for effective ligand interaction. The primary interactions were those due to van der Waals forces with limited electrostatic contributions. Immunochemical binding assay revealed that prior exposure to ligand **solutions** reduced the extent of antibody binding to **collagen**. Endotherms of modulated DSC scans also revealed significant differences in the enthalpy associated with the breakdown of triple helix and hydration networks of **collagen** in the absence and presence of ligands. The computational and analytical results thus present a consistent picture of ligand mediated interaction effects.  
CC Z Combined Coverage; C4 Chemical and Electrochemical Properties; Z-C4  
CT Conference Paper; Journal Article; Binding; Computer simulation; Networks; Biomedical materials; Mathematical models; Assaying; Organic compounds; Surgical implants; Biocompatibility  
ET D

=> d 123 all 2-10

L23 ANSWER 2 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2003(7):C4-P-519 EMA  
TI Comparative study of apatite formation on natural and synthetic polyamide in a mimicking **solution** to body fluid.  
AU Inada, H. (Nara Advanced Institute of Science and Technology); Ohtsuki, C. (Nara Advanced Institute of Science and Technology); Miyazaki, T. (Nara Advanced Institute of Science and Technology); Ogata, S. (Nara

PROberts

Advanced Institute of Science and Technology); Tanihara, M. (Nara Advanced Institute of Science and Technology)

SO Switzerland. 2003 Spectra, Diffraction Patterns, Photomicrographs, Numerical Data, 6 ref.. p. 15-18

Conference: Bioceramics 15: 15th International Symposium on Ceramics in Medicine at the Annual Meeting of the International Society for Ceramics in Medicine, Sydney, Australia, 4-8 Dec 2002

DT Conference Article

CY Switzerland

LA English

AB Natural bone is a kind of organic-inorganic hybrid composed of apatite and **collagen** fibers. Apatite-polymer hybrid is therefore expected to produce a novel material having both ability of bone-**bonding**, i.e. bioactivity, and mechanical properties analogous to natural bone. Biomimetic process has been paid much attention on fabrication of such hybrid, where bone-like apatite is deposited on polymer substrates in a simulated body fluid (SBF) with ion **concentrations** nearly equal to those of human extracellular fluid or more supersaturated fluids with respect to the apatite at ambient conditions. It has been revealed that carboxyl groups on organic polymer are effective for inducing heterogeneous nucleation of apatite in body environment. In the present study, apatite-forming ability of some natural polyamides, such as egg shell membrane and raw silk, and synthetic polyamide was examined in a **solution** mimicking body fluid. Apatite was formed on the raw silk after soaking in 1.5 SBF at pH 7.25 for 7 days, but not on egg shell membrane and synthetic polyamide, which have almost same contents or more of carboxyl groups compared to the raw silk. These results indicate that the apatite formation is governed not only by contents of carboxyl groups, but also by three-dimensional structure of the polyamides.

CC P Polymers; C4 Chemical and Electrochemical Properties; P-C4

CT Conference Paper; Polyamide resins; Surface properties; Fluids; Biocompatibility; Surface chemistry; Nucleation; Apatite; Substrates; Biomedical materials

L23 ANSWER 3 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2003(7):D1-D-1346 EMA

TI Apatite formation on polyamide films containing sulfonic groups by biomimetic process.

AU Kawai, T. (Nara Advanced Institute of Science and Technology); Miyazaki, T. (Nara Advanced Institute of Science and Technology); Ohtsuki, C. (Nara Advanced Institute of Science and Technology); Tanihara, M. (Nara Advanced Institute of Science and Technology); Nakao, J. (Toyobo); Sakaguchi, Y. (Toyobo); Konagaya, S. (Toyobo)

SO Switzerland. 2003 Photomicrographs, Diffraction Patterns, 6 ref.. p. 59-62

Conference: Bioceramics 15: 15th International Symposium on Ceramics in Medicine at the Annual Meeting of the International Society for Ceramics in Medicine, Sydney, Australia, 4-8 Dec 2002

DT Conference Article

CY Switzerland

LA English

AB Fabrication of apatite-polymer hybrids have been attractive to produce novel bone-repairing materials with both bone-**bonding** ability, i.e. bioactivity, and mechanical properties analogous to natural bone, since natural bone is a kind of organic-inorganic hybrid, composed of **collagen** fiber and apatite crystals. We previously reported that apatite was deposited on polyamide films containing carboxyl groups in a **solution** mimicking body fluid, when they were incorporated with



calcium salts. To find alternative functional group effective on the apatite formation, in the present study we examined apatite-forming ability on polyamide films containing sulfonic groups in the same **solution**. It was found that the polyamide film containing sulfonic groups could deposit apatite on the surfaces in the **solution** when the film was incorporated with calcium salts. These results show that sulfonic group also acts as a functional group effective for apatite deposition in body environment as carboxyl group. (Biomimetic process.)

CC D Composites; D1 Raw Materials; D-D1

CT Conference Paper; Apatite; Films; Polyamide resins; Functional groups; Composite materials; Biomedical materials; Development

L23 ANSWER 4 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2003(1):E6-Z-10 EMA

TI Effect of heat treatment on compressive strength and setting behavior of TTCP/DCPA-derived calcium phosphate **cement**.

AU Chen, W.C. (National Cheng Kung University); Ju, C.P. (National Cheng Kung University); Lin, J.H.C. (National Cheng Kung University)

SO Journal of Materials Science Letters (15 Oct. 2002) 21, (20) Diffraction Patterns, Graphs, 16 ref. p. 1583-1585

ISSN: 0261-8028

DT Journal

CY United States

LA English

AB As early as 1983, Brown and Chow indicated that mixtures of tetracalcium phosphate (TTCP) and di-calcium phosphate anhydrous (DCPA) powders in a diluted phosphate-containing **solution** led to the formation of hydroxyapatite (HA). According to this chemical reaction, a calcium phosphate **cement** (CPC) was first developed and patented in 1986. Thereafter, the use of this moldable CPC as bone substitute has attracted a great deal of attention and a variety of fabrication methods have been proposed. Different approaches have been reported to shorten the setting time of CPC. Examples include increasing the phosphate hardening **solution concentration**, using different hardening **solutions**, and mixing in calcium phosphate powders with such additives as HA, CaO, Na<sub>2</sub>O, P<sub>2</sub>O<sub>5</sub>, MgO, CaF<sub>2</sub> and **collagen**. Nevertheless, these modifications are often accompanied by sacrifices in biocompatibility and/or mechanical strength. The present work is an attempt to provide a simple heat treatment method that can modify the working/setting time of TTCP/DCPA-derived CPC without using additives or sacrificing its strength.

CC Z Combined Coverage; E6 Heat Treatment; Z-E6

CT Journal Article; Biomedical materials: Development; Bone **cements**; Calcium phosphate; Setting (hardening); Heat treatment; Compressive strength; Biocompatibility

ET Ca\*O; CaO; Ca cp; cp; O cp; Na\*O; Na<sub>2</sub>O; Na cp; O\*P; P<sub>2</sub>O<sub>5</sub>; P cp; Mg\*O; MgO; Mg cp; Ca\*F; CaF<sub>2</sub>; F cp

L23 ANSWER 5 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2003(1):E7-C-134 EMA

TI The interactions of bisphosphonates in **solution** and as coatings on hydroxyapatite with osteoblasts.

AU Ganguli, A. (University of Strathclyde); Henderson, C. (University of Strathclyde); Grant, M.H. (University of Strathclyde); Meikle, S.T. (University of Brighton); Lloyd, A.W. (University of Brighton); Goldie I. (Royal Academy of Medicine (Sweden))

SO Journal of Materials Science: Materials in Medicine (Oct. 2002) 13, (10) Spectra, Graphs, Photomicrographs, 24 ref. p. 923-931

PROBERTS

ISSN: 0957-4530

DT Journal  
CY United States  
LA English  
AB

Aseptic loosening is one of the major causes of failure of artificial hip joints, and it can occur for several reasons, including osteolysis of the bone tissue in response to stress shielding or cellular reactions to wear debris. Any treatment of the prosthesis which could minimize the osteolytic response of bone tissue may be able to extend the life-time of the implant. Bisphosphonates are potent inhibitors of osteoclastic bone resorption, and they bind avidly to hydroxyapatite (HA). Coating the prostheses with bisphosphonates may therefore inhibit osteolysis. We have investigated the potential for this approach by determining whether bisphosphonates interact with osteoblasts in vitro. The effects of pamidronate (P), clodronate (C), and etidronate (E) in **solution** and when coated onto HA were investigated. P inhibited protein and **collagen** syntheses potentially when in **solution**, but not after being bound to HA. When bound to HA, both P and C increased DNA, protein and **collagen** syntheses of osteoblasts and may encourage the osseointegration of implants. The pharmacological effects of the bisphosphonates studied altered dramatically after binding to HA. This must be fully investigated before this approach to prolonging prostheses stability can be evaluated.

CC C Ceramics; E7 Surface Finishing; C-E7  
CT Journal Article; Hydroxyapatite; Surgical implants; Prosthetics;  
Protective coatings; Binders (**adhesives**); Inhibitors  
ET P; C

L23 ANSWER 6 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2002(9):C4-D-447 EMA

TI In vivo estimation of calcium phosphate **cements** containing chondroitin sulfate in subcutis.

AU Yoshikawa, M. (Osaka Dental University); Hayami, S. (Osaka Dental University); Toda, T. (Osaka Dental University)

SO Switzerland. 2002 Photomicrographs, Diffraction Patterns, 23 ref.. p. 135-141

Conference: International Conference on Materials for Advanced Technologies: Symposium B: Biomaterials and Tissue Engineering., Singapore, Singapore, 1-6 July 2001

DT Conference Article  
CY Switzerland  
LA English  
AB

Calcium phosphate **cements** using an equimolar mixture of tetracalcium phosphate and dicalcium phosphate dihydrate (TeDCPD) for the powder phase were experimentally developed for use in endodontic treatment. The fundamental **cement** is composed of TeDCPD kneaded with modified McIlvaine's buffer **solution** containing calboxymethyl cellulose sodium salt (CEM-1). In the liquid phase of the modified one (CEM-2), chondroitin sulfate (CS) was added in place of the salt. The final **concentration** of CS in CEM-2 is 1%. Another one (CEM-3) contained 2% CS finally in place of the salt. X-ray diffract meter (XRD) was used to examine the crystalline phases of the **cements**. The tissue compatibility of the **cements** was examined histologically in the subcutaneous tissue using rats. The XRD results showed no dibasic calcium phosphate phase to be traced in CS containing two **cements** after 1 day of kneading. There were more multinucleated giant cells appearing around CEM-1 than around CEM-2 or CEM-3 after 4 weeks. Fibroblasts, **collagen** fibers and small vessels infiltrated into the internal porous structure of CEM-3.

PROberts

Excluding CEM-3, two **cements** were encapsulated with a dense fibrous connective tissue layer. We conclude that CS, in the experimentally developed **cement**, contributed to biocompatibility and bioactivity of the **cement**.

CC D Composites; C4 Chemical and Electrochemical Properties; D-C4  
CT Conference Paper; Bone **cements**: Surface properties; Surface chemistry: Biological effects; Biocompatibility; In vivo tests; Biomedical materials: Materials selection  
ET C\*D\*P\*Te; TeDCPD; Te cp; cp; D cp; C cp; P cp; C\*S; CS; S cp

L23 ANSWER 7 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2002(9):C4-D-423 EMA

TI Modification of biocement D-**collagen** I-composites with osteocalcin.

AU Reinstorf, A. (Technische Universitat Dresden); Knepper-Nicolai, B. (Technische Universitat Dresden); Hempel, U. (Institut fur Physiologische Chemie); Wenz, R. (Merck); Pompe, W. (Technische Universitat Dresden)

SO ISTECCNR, Via Granarolo n. 64, Faenza, 48018, Italy. 2002

Photomicrographs, Graphs, 17 ref.. p. 131-136

Conference: 7th Meeting and Seminar on: Ceramics, Cells and Tissues, Faenza, Italy, 13-15 June 2001

DT Conference Article

CY Italy

LA English

AB In order to generate a calcium-phosphate bone **cement** as a transient replacement for bone defects, Biocement D (Merck Biomaterial GmbH) containing mineralised **collagen** [1] was modified with osteocalcin. It was added to the **cement** paste during setting in order to control the crystallization kinetics of hydroxyapatite (HAP) as well as to stimulate the interactions between bone cells and between cells and the bone replacement material. Analysis by SEM shows, that osteocalcin causes a nanosize micro-structure of the **cement**. That can be explained by inhibited growth of HAP crystals. Mechanical measurements of compressive strength show a decrease by incorporation of osteocalcin, pointing onto a higher defect **concentration** of the crystalline structure. The influence of osteocalcin onto the interaction of bone cells with Biocement D-**Collagen** I-Composites was studied in a cell culture system using the human osteosarcoma cell line SAOS-2. Results suggest, that osteocalcin might improve the initial adherence of osteoblast-like cells.

CC D Composites; C4 Chemical and Electrochemical Properties; D-C4

CT Conference Paper; Bone **cements**: Surface properties; Hydroxyapatite: Composite materials; Organic compounds: Composite materials; Surface chemistry: Biological effects; Biocompatibility; Crystallization; Compressive strength; Biomedical materials: Materials selection

ET D; I

L23 ANSWER 8 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 2001(6):C1-D-1947 EMA

TI Hydroxyapatite-based materials for replacement of bone in load bearing situations.

AU Milthorpe, B. (University of New South Wales)

SO National University of Singapore, 30 Lower Kent Ridge Crescent, 119075, Singapore. 2000 Numerical Data, 22 ref.. p. 38-39

Conference: Tenth International Conference on Biomedical Engineering, , Singapore, 6-9 Dec. 2000

DT Conference Article

CY Singapore

PROberts

LA English

AB The majority of the compressive, tensile and torsional stresses borne by structural bone are taken by the cortical (or compact) bone. Bone replacement requires the quickest possible restoration of adequate strength on all three modes of loading. Calcium phosphate based materials generally show excellent bone compatibility and apposition with 'biological' **bonding** between the material and the healing bone. These materials, however, have poor fracture toughness and a relatively high elastic modulus compared to cortical bone and may also be weak in porous forms. **Solutions** to these problems have been many and varied. Hydroxyapatite (HAp) has been used as a coating material where, hopefully, the stresses are mostly in shear or compression. HAp and bioglass particles have been included as bio-active fillers in a variety of matrices including polyethylene; poly-lactide/glycolide and **collagen**: The other major strategy has been to reinforce the HAp matrix with fibres, or ceramic particles.

CC D Composites; C1 Mechanical Properties; D-C1

CT Conference Paper; Particulate composites: Mechanical properties; Polyethylenes: Composite materials; Hydroxyapatite: Composite materials; Glass ceramics: Composite materials; Compressive strength; Shear strength; Loading

L23 ANSWER 9 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 1999(10):A2-D-491 EMA

TI Pore and structure formation in collage-hydroxyapatite precursors: Experiment-model.

AU Lampenscherf, S. (Technische Universitat Dresden); Weis, K. (Technische Universitat Dresden); Pompe, W. (Technische Universitat Dresden)

SO Switzerland. 1999 Graphs, Photomicrographs, 9 ref.. p. 362-367  
Conference: Functionally Graded Materials 1998, Dresden, Germany, 26-29 Oct. 1998

DT Conference Article

CY Switzerland

LA English

AB In this paper we discuss different routes for the formation of **collagen/HAP-composites** with graded porosity. We show experimental evidence of the pore growth during phase separation of an aqueous **collagen solution** and investigate the influence of different mechanical boundary conditions (freestanding body, film on rigid substrate). The formation of a graded pore structure via phase separation is presented as well as the successful synthesis of a **collagen/HAP-composite** via a **cementation** reaction from a colloidal HAP-precursor. In the modelling part we focus on the drying process as a route for graded densification and structure formation. We present a brief description of the model used to investigate stress formation and plastic deformation in a two-phase material containing a liquid and a solid phase. We outline the important processing and material parameters for structural design and show how the model can be used to find the optimum processing conditions for a desired graded structure.

CC D Composites; A2 Microstructure; D-A2

CT Conference Paper; Hydroxyapatite: Composite materials; Functionally gradient materials: Microstructure; Pore formation; Porosity; Phase separation

L23 ANSWER 10 OF 10 EMA COPYRIGHT 2003 CSA on STN

AN 1994(7):D2-C-1031 EMA

TI A New Bioglass Ceramic.

AU Arif I. (Punjab University)

PRoberts

SO Dr. A.Q. Khan Research Laboratories, Kahuta, P.O. Box 502, Rawalpindi, Pakistan. 1994 Photomicrographs, Diffraction Patterns, 15 ref.. p. 127-132  
Conference: Advanced Materials-93, Islamabad, Pakistan, 20-24 Sept. 1993  
See also AN: 94(7):G2-Z-175

DT Conference Article

CY Pakistan

LA English

AB Since the discovery of Bioglass by Hench et al ., various kinds of glasses and glass-ceramics have been discovered to bond to living bone. Their mechanical properties, of course, have not been very good. Therefore, their applications have been limited to low load-bearing parts. The natural bone is a composite of small spastite particles reinforced by **collagen**. A new bioglass-ceramic:  $\text{MgO-CaO-P sub 2 O sub 5 -SiO sub 2 -TiO sub 2 B sub 2 O sub 3 -Na sub 2 O-ZrO sub 2 -CaF sub 2}$  of improved mechanical and other properties has been developed. Optical microscopy revealed uniform crystals of 25  $\mu\text{m}$  size. In addition, a bioactive bone **cement** based on  $\text{CaO-SiO sub 2 -P sub 2 O sub 5}$  glass powder in ammonium phosphate **solution** has also been developed. The **cement** dried within a few minutes after application and formed a strong bond with the natural living bone. The dog tibia tests of the glass-ceramic and the bioactive **cement** showed that the materials were biocompatible and the biocement formed strong chemical bond with the living bone.

CC C Ceramics; D2 Materials Development; C-D2

CT Conference Paper; Glass ceramics: Development; Biocompatibility; Surgical implants: Materials selection; Triclinic lattice

ET  $\text{Ca*Mg*O*P}$ ; Ca sy 4; sy 4; Mg sy 4; O sy 4; P sy 4; MgO; Mg cp; cp; O cp; CaO; Ca cp; MgO-CaO-P; O; O\*Si; SiO; Si cp; O\*Ti; TiO; Ti cp; Na; O\*Zr; ZrO; Zr cp; O-ZrO; Ca\*F; CaF; F cp; Ca\*O\*Si; Ca sy 3; sy 3; O sy 3; Si sy 3; CaO-SiO; P

=>